Primary Cilia Integrate Hedgehog and Wnt Signaling during Tooth Development.

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Public Summary:
Wnt signaling is critical for the development and homeostasis of the dentition, and in this work we demonstrate the consequences of aberrant Wnt signaling on how the teeth form. These data lay the foundation for our ongoing work using Wnt proteins to stimulate dentin repair.

Scientific Abstract:
Many ciliopathies have clinical features that include tooth malformations but how these defects come about is not clear. Here we show that genetic deletion of the motor protein Kif3a in dental mesenchyme results in an arrest in odontogenesis. Incisors are completely missing, and molars are enlarged in Wnt1(Cre+)Kif3a(fl/fl) embryos. Although amelogenesis and dentinogenesis initiate in the molar tooth bud, both processes terminate prematurely. We demonstrate that loss of Kif3a in dental mesenchyme results in loss of Hedgehog signaling and gain of Wnt signaling in this same tissue. The defective dental mesenchyme then aberrantly signals to the dental epithelia, which prompts an up-regulation in the Hedgehog and Wnt responses in the epithelia and leads to multiple attempts at invagination and an expanded enamel organ. Thus, the primary cilium integrates Hedgehog and Wnt signaling between dental epithelia and mesenchyme, and this cilia-dependent integration is required for proper tooth development.